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FILE 'HOME' ENTERED AT 09:56:48 ON 30 MAY 2009

=> FIL REGISTRY
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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=> E "REVERSE TRANSCRIPTASE"/CN 25
E1            1     REVERSE OSTEOGENIC GROWTH PEPTIDE/CN
E2            1     REVERSE T3/CN
E3            1 --> REVERSE TRANSCRIPTASE/CN
E4            1     REVERSE TRANSCRIPTASE (ADINETA VAGA CLONE AVC1 TRANSPOSON ATHENA
FRAGMENT)/CN
E5            1     REVERSE TRANSCRIPTASE (ADINETA VAGA TRANSPOSON ATHENA-AV1
FRAGMENT)/CN
E6            1     REVERSE TRANSCRIPTASE (ADINETA VAGA TRANSPOSON ATHENA-AV2
FRAGMENT)/CN
E7            1     REVERSE TRANSCRIPTASE (ADINETA VAGA TRANSPOSON ATHENA-AV4
FRAGMENT)/CN
E8            1     REVERSE TRANSCRIPTASE (AEDES ALBOPICTUS C6/36 CELL FRAGMENT)/CN
E9            1     REVERSE TRANSCRIPTASE (ALTERNARIA ALTERNATA RETROTRANSPOSON REAL
GENE POL)/CN
E10           1     REVERSE TRANSCRIPTASE (ANDREAEA RUPESTRIS CLONE ANDRUPTY3-2
RETROTRANSPOSON GENE RT FRAGMENT)/CN
E11           1     REVERSE TRANSCRIPTASE (ANGUILLA JAPONICA CLONE AJA6-15
RETROTRANSPOSON UNAL2)/CN
E12           1     REVERSE TRANSCRIPTASE (ARABIDOPSIS THALIANA CLONE B4
RETROTRANSPOSON TA23 FRAGMENT)/CN
E13           1     REVERSE TRANSCRIPTASE (ARABIDOPSIS THALIANA CLONE T6B12 GENE
T6B12.3)/CN
E14           1     REVERSE TRANSCRIPTASE (ARABIDOPSIS THALIANA GENE AT2G02650)/CN
E15           1     REVERSE TRANSCRIPTASE (ARABIDOPSIS THALIANA GENE T4C9.20)/CN
E16           1     REVERSE TRANSCRIPTASE (BACILLUS CALDOLYTICUS STRAIN EA1 GENE
RECA GROUP II INTRON)/CN
E17           2     REVERSE TRANSCRIPTASE (BACILLUS CEREUS STRAIN ATCC10987 PLASMID
PBC10987)/CN
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E18          1     REVERSE TRANSCRIPTASE (BACILLUS CEREUS STRAIN F4810/72 PLASMID
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E19          1     REVERSE TRANSCRIPTASE (BACTEROIDES FRAGILIS STRAIN ATCC25285)/CN
E20          1     REVERSE TRANSCRIPTASE (BACTEROIDES FRAGILIS STRAIN YCH46)/CN
E21          1     REVERSE TRANSCRIPTASE (BACTEROIDES THETAIOTAOMICRON STRAIN
VPI-5482 GENE BT2297)/CN
E22          1     REVERSE TRANSCRIPTASE (BACTEROIDES THETAIOTAOMICRON STRAIN
VPI-5482 GENE BT2615)/CN
E23          1     REVERSE TRANSCRIPTASE (BACTEROIDES THETAIOTAOMICRON STRAIN
VPI-5482 GENE BT2617)/CN
E24          1     REVERSE TRANSCRIPTASE (BIOMPHALARIA GLABRATA STRAIN BS90 NON-LTR
RETROTRANSPOSON NIMBUS (BGI) SEQUENCE HOMOLOG FRAGMENT)/CN
E25          1     REVERSE TRANSCRIPTASE (BLUEBERRY RED RINGSPOT VIRUS)/CN

=> S E3
L1           1 "REVERSE TRANSCRIPTASE"/CN

=> sel L1 chem
E1 THROUGH E17 ASSIGNED

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     6.69       6.91

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 09:58:09 ON 30 MAY 2009

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s e1-e17 (s) (mn or manganese)
          1   FILE ADISCTI
          2   FILE ADISINSIGHT
          2   FILE ADISNEWS
         39   FILE AGRICOLA
          1   FILE ANABSTR
          2   FILE AQUALINE
          8   FILE AQUASCI
         23   FILE BIOENG
   9 FILES SEARCHED...
         64   FILE BIOSIS
         50   FILE BIOTECHABS
         50   FILE BIOTECHDS
        144   FILE BIOTECHNO
  13 FILES SEARCHED...
         32   FILE CABA
        110   FILE CAPLUS
  15 FILES SEARCHED...
          8   FILE CEABA-VTB
          3   FILE CIN
          7   FILE DDFU
       3806   FILE DGENE
  23 FILES SEARCHED...
         11   FILE DISSABS
         22   FILE DRUGU
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        80   FILE EMBASE
       144   FILE ESBIOBASE
  33 FILES SEARCHED...
         3   FILE FSTA
       623   FILE GENBANK
  35 FILES SEARCHED...
        78   FILE IFIPAT
       160   FILE LIFESCI
        53   FILE MEDLINE
        12   FILE NTIS
         1   FILE OCEAN
        82   FILE PASCAL
  47 FILES SEARCHED...
  48 FILES SEARCHED...
         3   FILE PHAR
        18   FILE PROMT
         1   FILE PROUSDDR
        34   FILE SCISEARCH
        26   FILE TOXCENTER
       276   FILE USGENE
  59 FILES SEARCHED...
       664   FILE USPATFULL
         2   FILE USPATOLD
       105   FILE USPAT2
  62 FILES SEARCHED...
         1   FILE VETU
         2   FILE WATER
        57   FILE WPIDS
  67 FILES SEARCHED...
        57   FILE WPINDEX

  43 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L2   QUE ("CYSCRIBE REVERSE TRANSCRIPTASE"/BI OR CYSCRIPT/BI OR "E.C. 2.7.7.49"
         /BI OR "REVERSE TRANSCRIPTASE POLYMERASE"/BI OR "REVERSE TRANSCRIPTASE
         "/BI OR REVERTASE/BI OR "RNA REVERTASE"/BI OR "RNA-DEPENDENT DEOXYRIBO
         NUCLEATE NUCLEOTIDYLTRANSFERASE"/BI OR "RNA-DEPENDENT DNA POLYMERASE"/
         BI OR "RNA-DIRECTED DNA POLYMERASE"/BI OR "RNA-INSTRUCTED DNA POLYMERA
         SE"/BI OR RTIS/BI OR "SUPERSCRIPT II"/BI OR SUPERSCRIPT/BI OR "THERMOS
         CRIPT II"/BI OR THERMOSCRIPT/BI OR 9068-38-6/BI) (S) (MN OR MANGANESE)


=> s L2 (s) (intracellular or cellular or cytoplas###)
         1   FILE ADISNEWS
         7   FILE AGRICOLA
         1   FILE ANABSTR
         1   FILE AQUALINE
         5   FILE BIOENG
         2   FILE BIOTECHABS
  11 FILES SEARCHED...
         2   FILE BIOTECHDS
        16   FILE BIOTECHNO
  13 FILES SEARCHED...
         2   FILE CABA
         1   FILE CAPLUS
  15 FILES SEARCHED...
         2   FILE CEABA-VTB
         1   FILE CIN
        22   FILE DGENE
  23 FILES SEARCHED...
         1   FILE DISSABS
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         2   FILE EMBASE
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  35 FILES SEARCHED...
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        17   FILE LIFESCI
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         1   FILE SCISEARCH
        76   FILE USGENE
  59 FILES SEARCHED...
        38   FILE USPATFULL
         2   FILE USPAT2
         1   FILE WATER
  67 FILES SEARCHED...

  28 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L3   QUE L2 (S) (INTRACELLULAR OR CELLULAR OR CYTOPLAS###)

=> s L3 and (inhibit### or modulat### or increas### or decreas### or elevat###)
         1   FILE ADISNEWS
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         1   FILE ANABSTR
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         1   FILE EMBASE
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        17   FILE ESBIOBASE
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         1   FILE MEDLINE
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  47 FILES SEARCHED...
  48 FILES SEARCHED...
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         1   FILE SCISEARCH
  58 FILES SEARCHED...
        34   FILE USPATFULL
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         2   FILE USPAT2
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          1   FILE WATER
  66 FILES SEARCHED...

  25 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L4   QUE L3 AND (INHIBIT### OR MODULAT### OR INCREAS### OR DECREAS### OR ELEVAT
       ###)

=> d rank
F1         505   GENBANK
F2          34   USPATFULL
F3          17   ESBIOBASE
F4          13   LIFESCI
F5          11   BIOTECHNO
F6          11   PASCAL
F7           6   AGRICOLA
F8           2   BIOENG
F9           2   CABA
F10          2   USPAT2
F11          1   ADISNEWS
F12          1   ANABSTR
F13          1   AQUALINE
F14          1   BIOTECHABS
F15          1   BIOTECHDS
F16          1   CAPLUS
F17          1   CIN
F18          1   DISSABS
F19          1   EMBASE
F20          1   FSTA
F21          1   IFIPAT
F22          1   MEDLINE
F23          1   PROMT
F24          1   SCISEARCH
F25          1   WATER


=> fil f3-f5, f7-f9, f11-f25
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                19.04      25.95

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   2 FILES SEARCHED...
   3 FILES SEARCHED...
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  17 FILES SEARCHED...
  19 FILES SEARCHED...
L5          65 L4

=> dup rem L5
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ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L5
L6           48 DUP REM L5 (17 DUPLICATES REMOVED)

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   6 FILES SEARCHED...
  12 FILES SEARCHED...
  18 FILES SEARCHED...
L7          25 L6 AND PY<2004

=> d L7 ibib abs 1-15

L7     ANSWER 1 OF 25 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on
       STN
ACCESSION NUMBER:       2003273684   ESBIOBASE <<LOGINID::20090530>>
TITLE:                  Cholesterol Depletion Impairs Vascular Reactivity to
                        Endothelin-1 by Reducing Store-Operated Ca 2+  Entry
                        Dependent on TRPC1
AUTHOR(S):              Bergdahl, Andreas; Gomez, Maria F.; Dreja, Karl; Adner,
                        Mikael; Broman, Jonas; Hellstrand, Per; Sward, Karl;
                        Xu, Shang-Zhong; Beech, David J.
CORPORATE SOURCE:       Bergdahl, Andreas; Gomez, Maria F.; Dreja, Karl; Adner,
                        Mikael; Broman, Jonas; Hellstrand, Per; Sward, Karl
                        (Department of Physiological Sciences, Lund University,
                        Lund (SE)); Sward, Karl (Department of Physiological
                        Sciences, Lund University, BMC F12, S-21 84 Lund (SE));
                        Xu, Shang-Zhong; Beech, David J.
                        EMAIL: karl.sward@mphy.lu.se
SOURCE:                 Circulation Research (31 Oct 2003) Volume 93,
                        Number 9, pp. 839-847, 30 refs.
                        CODEN: CIRUAL  ISSN: 0009-7330
                        DOI: 10.1161/01.RES.0000100367.45446.A3
COUNTRY OF PUBLICATION: United States of America
DOCUMENT TYPE:          Journal; Article
LANGUAGE:               English
SUMMARY LANGUAGE:       English
ENTRY DATE:             Entered STN: 2 Feb 2009
                        Last updated on STN: 2 Feb 2009
AN     2003273684   ESBIOBASE <<LOGINID::20090530>>
AB     The reactivity of the vascular wall to endothelin-1 (ET-1) is influenced
       by cholesterol, which is of possible importance for the progression of
       atherosclerosis. To elucidate signaling steps affected, the cholesterol
       acceptor methyl-β-cyclodextrin (mβcd, 10 mmol/L) was used to
       manipulate membrane cholesterol and disrupt caveolae in intact rat
       arteries. In endothelium-denuded caudal artery, contractile
       responsiveness to 10 nmol/L ET-1 (mediated by the ET A  receptor) was
       reduced by mβcd and  increased by cholesterol. Neither
       ligand binding nor colocalization of ET  A  and caveolin-1 was affected
       by mβcd. Ca 2+  inflow via store-operated channels after depletion
       of intracellular Ca 2+  stores was reduced in
       mβcd-treated caudal arteries, as shown by  Mn  2+  quench
       rate and intracellular [Ca 2+ ] response. Expression of TRPC1,
       3, and 6 was detected by reverse transcriptase-
       polymerase chain reaction, and colocalization of TRPC1 with
       caveolin-1 was reduced by mβcd, as seen by immunofluorescence. Part
       of the contractile response to ET-1 was inhibited by Ni 2+
       (0.5 mmol/L) and by a TRPC1 blocking antibody. In the basilar artery,
       exhibiting less store-operated channel activity than the caudal artery,
       ET-1-induced contractions were insensitive to the TRPC1 blocking
       antibody and to mβcd.  Increased store-operated channel
       activity in basilar arteries after organ culture correlated with
       increased sensitivity of ET-1 contraction to mβcd. These
       results suggest that cholesterol influences vascular reactivity to ET-1
       by affecting the caveolar localization of TRPC1.

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STN

ACCESSION NUMBER: 2003205687 ESBIOBASE <<LOGINID::20090530>>

TITLE: Cloning and characterization of a mouse endoplasmic reticulum alkaline ceramidase. An enzyme that preferentially regulates metabolism of very long chain ceramides

AUTHOR(S): Mao, Cungui; Xu, Ruijuan; Hu, Wei; Obeid, Lina M.; Szulc, Zdzislaw M.; Bielawski, Jacek; Beeker, Kevin P.; Bielawska, Alicja; Galadari, Sehamuddin H.

CORPORATE SOURCE: Mao, Cungui; Xu, Ruijuan; Hu, Wei; Obeid, Lina M. (Department of Medicine, Medical University of South Carolina, Charleston, SC 29425 (US)); Mao, Cungui; Obeid, Lina M. (Div. of General Internal Medicine, 114 Doughty St., Charleston, SC 29425 (US)); Hu, Wei; Obeid, Lina M.; Szulc, Zdzislaw M.; Bielawski, Jacek; Beeker, Kevin P.; Bielawska, Alicja (Dept. of Biochem. and Molec. Biology, Medical University of South Carolina, Charleston, SC 29425 (US)); Obeid, Lina M. (Ralph H. Johnson Vet. Admin. Hosp., Medical University of South Carolina, Charleston, SC 29425 (US)); Galadari, Sehamuddin H. (Department of Biochemistry, Fac. of Medicine and Health Sciences, United Arab Emirates University, Al Ain (AE))

EMAIL: maoc@musc.edu; obeidl@musc.edu

SOURCE: Journal of Biological Chemistry (15 Aug 2003) Volume 278, Number 33, pp. 31184-31191, 30 refs.

CODEN: JBCHA3 ISSN: 0021-9258

DOI: 10.1074/jbc.M303875200

COUNTRY OF PUBLICATION: United States of America

DOCUMENT TYPE: Journal; Article

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Feb 2009

Last updated on STN: 2 Feb 2009

AN 2003205687 ESBIOBASE <<LOGINID::20090530>>

AB Ceramidases deacylate ceramides, important intermediates in the metabolic pathway of sphingolipids. In this study, we report the cloning and characterization of a novel mouse alkaline ceramidase (maCER1) with a highly restricted substrate specificity. maCER1 consists of 287 amino acids, and it has a 28 and 32% identity to the Saccharomyces alkaline ceramidases (YPC1p and YDC1p) and the human alkaline phytoceramidase, respectively. Reverse transcriptase-PCR analysis demonstrated that maCER1 was predominantly expressed in skin. maCER1 was localized to the endoplasmic reticulum as revealed by immunocytochemistry. In vitro biochemical characterization determined that maCER1 hydrolyzed D-erythro-ceramide exclusively but not D-erythro-dihydroceramide or D-ribo-phytoceramide. Similar to other alkaline ceramidases, maCER1 had an alkaline pH optimum of 8.0, and it was activated by Ca 2+ but inhibited by Zn 2+ , Cu 2+ , and Mn 2+ . maCER1 was also inhibited by sphingosine, one of its products. Metabolic labeling studies showed that overexpression of maCER1 caused a decrease in the incorporation of radiolabeled dihydrosphingosine into ceramide and complex sphingolipids but led to a concomitant increase in sphingosine-1-P (S1P) in HeLa cells. Mass measurement showed that overexpression of maCER1 selectively lowered the cellular levels of D-erythro-C 24:1 -ceramide, but not other ceramide species and caused an increase in the levels of S1P. Taken together, these data suggest that maCER1 is a novel alkaline ceramidase with a stringent substrate specificity and that maCER1 is selectively expressed in skin and may have a role in regulating the levels of bioactive lipids ceramide and S1P, as well as

complex sphingolipids.

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ACCESSION NUMBER: 2002090875 ESBIOBASE <<LOGINID::20090530>>
TITLE: Scavenger receptor class B type I expression and elemental analysis in cerebellum and parietal cortex regions of the Alzheimer's disease brain
AUTHOR(S): Srivastava, Rai Ajit K.; Jain, Jinesh C.
CORPORATE SOURCE: Srivastava, Rai Ajit K. (Washington University, School of Medicine, Saint Louis, MO 63110 (US)); Srivastava, Rai Ajit K. (Cellular and Molecular Biology, Esperion Therapeutics Inc., 3621 S State Street, 695 KMS Place, Ann Arbor, MI 48108 (US)); Jain, Jinesh C. (Department of Civil Engineering and Geological Sciences, University of Notre Dame, Notre Dame, IN 46556 (US)) EMAIL: ajits@esperion.com
SOURCE: Journal of the Neurological Sciences (15 Apr 2002) Volume 196, Number 1-2, pp. 45-52, 51 refs. CODEN: JNSCAG ISSN: 0022-510X DOI: 10.1016/S0022-510X(02)00026-6
PUBL. ITEM IDENTIFIER: S0022510X02000266
COUNTRY OF PUBLICATION: Netherlands
DOCUMENT TYPE: Journal; (Conference Paper)
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2002090875 ESBIOBASE <<LOGINID::20090530>>
AB Metal ions play an important role in health and disease by influencing cellular biochemical pathways. The increased concentrations of some metal ions may have cytotoxic effects through their ability to oxidatively modify biomolecules, which may cause oxidative stress-induced brain cell death leading to neurodegenerative disorders observed in Alzheimer's disease (AD). We therefore performed elemental analysis of human brain tissues by a sophisticated method of inductively coupled plasma mass spectrometry (ICP-MS) in two regions of the AD brain, the parietal cortex and cerebellum, and compared them with the age-matched control. Our analysis shows the differential distribution of some metal ions in the two regions of the brain. Most importantly, Si, Sn, Al and Mn showed significantly higher levels in the parietal cortex of the AD brain compared to the control. The other metal ions showing moderate increases in the parietal cortex were Na, Te, Cr, Fe and B. Since these metal ions can modify lipoproteins in the brain and modified lipoproteins are taken up by scavenger receptors class B type I (SR-BI), we also determined the presence of SR-BI in the parietal cortex and cerebellum regions of the control and AD brains using a sensitive method, the reverse transcriptase-polymerase chain reaction. Our results suggest that SR-BI are present in the parietal cortex as well as in the cerebellum of the control and AD brains, suggesting that the presence of SR-BI may be involved in the uptake of oxidatively modified lipoproteins and β-amyloid (Aβ) protein complexed with apoE, suggesting implications in the progression of late onset AD and other neurodegenerative disorders characterized by the deposition of insoluble aggregates observed in the AD brain. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L7 ANSWER 4 OF 25 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2002061673 ESBIOBASE <<LOGINID::20090530>>

TITLE: Homocysteine induces 3-hydroxy-3-methylglutaryl coenzyme a reductase in vascular endothelial cells: A mechanism for development of atherosclerosis?
AUTHOR(S): Li, Hong; Lewis, Avalyn; Brodsky, Sergey; Rieger, Robert; Iden, Charles; Goligorsky, Michael S.
CORPORATE SOURCE: Li, Hong; Lewis, Avalyn; Brodsky, Sergey; Rieger, Robert; Iden, Charles; Goligorsky, Michael S. (Department of Medicine, State University of New York, Stony Brook, NY 11794-8152 (US))
SOURCE: Circulation (5 Mar 2002) Volume 105, Number 9, pp. 1037-1043, 35 refs.
CODEN: CIRCAZ ISSN: 0009-7322
DOI: 10.1161/hc0902.104713
COUNTRY OF PUBLICATION: United States of America
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2002061673 ESBIOBASE <<LOGINID::20090530>>

AB Background - It has been established that hyperhomocyst(e)inemia (HHCy) is an independent and graded risk factor for atherosclerosis, although the molecular link to the atherosclerotic process remains obscure. Methods and Results - Screening human umbilical vein endothelial cells (HUVECs) with complementary DNA microarray for the gene expression modified by homocysteine (Hcy) revealed that 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) was upregulated. This effect was confirmed using quantitative reverse transcriptase-polymerase chain reaction. Actinomycin D studies revealed that Hcy stabilized HMGCR mRNA (τ 1/2 , 9.5±1.0 versus 5.0±0.2 hours). Expression of immunodetectable HMGCR in both HUVECs and renal microvascular endothelial cells was increased in Hcy-treated cells in association with the increased abundance of caveolin. Application of a cell-permeable superoxide dismutase mimetic, Mn -TBAP, reversed the Hcy-induced expression of HMGCR. Additional biochemical analysis of the abundance of total cellular cholesterol showed that 0, 20, 50, and 100 μmol/L Hcy resulted in 22.2±7.3%, 39.5±1.2%, and 50.4±6.8% increase, respectively. Gas chromatography mass spectrometry analysis of extracted cholesterol from Hcy-treated HUVECs and from the culture medium showed 17.8±5.2% and 24.0±14.5% increases, respectively. Application of simvastatin to Hcy-treated cells reduced cellular cholesterol and prevented Hcy-induced suppression of NO production by HUVECs in a dose-dependent manner. Conclusions - Using a cDNA microarray, the data disclosed an unexpected link between Hcy and cholesterol dysregulation based on the finding of increased abundance of HMGCR mRNA and protein in endothelial cells, demonstrated the possible role of Hcy-induced oxidative stress in this response, and revealed the improvement of endothelial NO production in Hcy-treated HUVECs by statins. Collectively, these findings may provide a solid explanation for the observed proatherogenic effect of HHcy.

L7 ANSWER 5 OF 25 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001215996 ESBIOBASE <<LOGINID::20090530>>
TITLE: A diacylglycerol-activated Ca 2+ channel in PC12 cells (an adrenal chromaffin cell line) correlates with expression of the TRP-6 (transient receptor potential) protein
AUTHOR(S): Tesfai, Y.; Brereton, H.M.; Barritt, G.J.
CORPORATE SOURCE: Tesfai, Y.; Brereton, H.M.; Barritt, G.J. (Department

of Medical Biochemistry, School of Medicine, Flinders University, G.P.O. Box 2100, Adelaide, SA 5001 (AU))

SOURCE: Biochemical Journal (15 Sep 2001) Volume 358, Number 3, pp. 717-726, 51 refs.
CODEN: BIJOAK ISSN: 0264-6021
DOI: 10.1042/0264-6021:3580717
COUNTRY OF PUBLICATION: United Kingdom
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2001215996 ESBIOBASE <<LOGINID::20090530>>

AB The structures, and mechanisms of activation, of plasma membrane intracellular-messenger-activated, non-selective cation channels in animal cells are not well understood. The PC12 adrenal chromaffin cell line is a well-characterized example of a nerve cell. In PC12 cells, 1-oleolyl-2-acetyl-sn-glycerol (OAG), a membrane-permeant analogue of diacylglycerol, initiated the inflow of Ca 2+ , Mn 2+ and Sr 2+ . Acetylcholine and thapsigargin initiated the inflow of Ca 2+ and Mn 2+ , but not of Sr 2+ . The activation of bivalent cation inflow by OAG: (i) was mimicked by another membrane-permeant diacylglycerol analogue, 1,2-dioctanoyl-sn-glycerol, but not by the membrane-impermeant analogue 1-stearoyl-2-arachidonyl-sn-glycerol; (ii) was not blocked by staurosporin or chelerythrine, inhibitors of protein kinase C; (iii) was enhanced by RHC80267 and R50922, inhibitors of diacylglycerol lipase and diacylglycerol kinase respectively; and (iv) was inhibited by extracellular Ca 2+ . When OAG was added after acetylcholine, the effect of OAG on Ca 2+ inflow was over-and-above that induced by acetylcholine. 2-Aminoethyl diphenylborate (2-APB) inhibited Ca 2+ inflow initiated by either acetylcholine or thapsigargin, but not that initiated by OAG. Flufenamic acid inhibited OAG-initiated, but not acetylcholine-initiated, Ca 2+ and Mn 2+ inflow. OAG-initiated Ca 2+ inflow was less sensitive to inhibition by SK&F96365 than acetylcholine-initiated Ca 2+ inflow. In poly polyadenylated RNA prepared from PC12 cells, mRNA encoding TRP (transient receptor potential) proteins 1-6 was detected by reverse transcriptase (RT)-PCR, and in lysates of PC12 cells the endogenous TRP-6 protein was detected by Western blot analysis. It is concluded that PC12 cells express a diacylglycerol-activated, non-selective cation channel. Expression of this channel function correlates with expression of the TRP-3 and TRP-6 proteins, which have been shown previously to be activated by diacylglycerol when expressed heterologously in animal cells [Hofmann, Obukhov, Schaefer, Harteneck, Gudermann, and Schultz (1999) Nature (London) 397, 259-263].

L7 ANSWER 6 OF 25 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2001188823 ESBIOBASE <<LOGINID::20090530>>

TITLE: Maitotoxin activates an endogenous non-selective cation channel and is an effective initiator of the activation of the heterologously expressed hTRPC-1 (transient receptor potential) non-selective cation channel in H4-IIE liver cells

AUTHOR(S): Brereton, Helen M.; Chen, Jinglong; Harland, M.Lyn; Barritt, Gregory J.; Rychkov, Grigori

CORPORATE SOURCE: Brereton, Helen M.; Chen, Jinglong; Harland, M.Lyn; Barritt, Gregory J. (Department of Medical

Biochemistry, School of Medicine, Flinders University, G.P.O. Box 2100, Adelaide, SA 5001 (AU)); Rychkov, Grigori (Centre for Advanced Biomedical Studies, University of South Australia and Department of Physiology, University of Adelaide, G.P.O. Box 498, Adelaide, SA 5001 (AU))
EMAIL: greg.barritt@flinders.edu.au
SOURCE: Biochimica et Biophysica Acta - Molecular Cell Research (22 Aug 2001) Volume 1540, Number 2, pp. 107-126, 53 refs.
CODEN: BAMRDP ISSN: 0167-4889
DOI: 10.1016/S0167-4889(01)00124-0
PUBL. ITEM IDENTIFIER: S0167488901001240
COUNTRY OF PUBLICATION: Netherlands
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2001188823 ESBIOBASE <<LOGINID::20090530>>

AB The structures and mechanisms of activation of non-selective cation channels (NSCCs) are not well understood although NSCCs play important roles in the regulation of metabolism, ion transport, cell volume and cell shape. It has been proposed that TRP (transient receptor potential) proteins are the molecular correlates of some NSCCs. Using fura-2 and patch-clamp recording, it was shown that the maitotoxin-activated cation channels in the H4-IIE rat liver cell line admit Ca 2+ , Mn 2+ and Na + , have a high selectivity for Na + compared with Ca 2+ , and are inhibited by Gd 3+ (half-maximal inhibition at 1 μM). Activation of the channels by maitotoxin was inhibited by increasing the extracellular Ca 2+ concentration or by inclusion of 10 mM EGTA in the patch pipette. mRNA encoding TRP proteins 1, 2 and 3 at levels comparable with those in brain was detected using reverse transcriptase-polymerase chain reaction in poly(A) + RNA prepared from H4-IIE cells and freshly-isolated rat hepatocytes. In H4-IIE cells transiently transfected with cDNA encoding hTRPC-1, the expressed hTRPC-1 protein was chiefly located at intracellular sites and at the plasma membrane. Cells expressing hTRPC-1 exhibited a substantial enhancement of maitotoxin-initiated Ca 2+ inflow and a modest enhancement of thapsigargin-initiated Ca 2+ inflow (measured using fura-2) and no enhancement of the highly Ca 2+ -selective store-operated Ca 2+ current (measured using patch-clamp recording). In cells expressing hTRPC-1, maitotoxin activated channels which were not found in untransfected cells, have an approximately equal selectivity for Na + and Ca 2+ , and are inhibited by Gd 3+ (half-maximal inhibition at 3 μM). It is concluded that in liver cells (i) maitotoxin initiates the activation of endogenous NSCCs with a high selectivity for Na + compared with Ca 2+ ; (ii) TRP proteins 1, 2 and 3 are expressed; (iii) maitotoxin is an effective initiator of activation of heterologously expressed hTRPC-1 channels; and (iv) the endogenous TRP-1 protein is unlikely to be the molecular counterpart of the maitotoxin-activated NSCCs nor the highly Ca 2+ -selective store-operated Ca 2+ channels.

L7 ANSWER 7 OF 25 LIFESCI COPYRIGHT 2009 CSA on STN
ACCESSION NUMBER: 2003:9314 LIFESCI <<LOGINID::20090530>>
TITLE: A diacylglycerol-activated Ca super(2+) channel in PC12 cells (an adrenal chromaffin cell line) correlates with expression of the TRP-6 (transient receptor potential) protein

AUTHOR: Tesfai, Y.; Brereton, H.M.; Barritt, G.J.*
CORPORATE SOURCE: Department of Medical Biochemistry, School of Medicine, Faculty of Health Sciences, Flinders University, G.P.O. Box 2100, Adelaide, South Australia, 5001, Australia; E-mail: Greg.Barritt@flinders.edu.au
SOURCE: Biochemical Journal [Biochem. J.], (20010915) vol. 358, no. 3, pp. 717-726.
ISSN: 0264-6021.
DOCUMENT TYPE: Journal
FILE SEGMENT: T
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The structures, and mechanisms of activation, of plasma membrane intracellular-messenger-activated, non-selective cation channels in animal cells are not well understood. The PC12 adrenal chromaffin cell line is a well-characterized example of a nerve cell. In PC12 cells, 1-oleolyl-2-acetyl-sn-glycerol (OAG), a membrane-permeant analogue of diacylglycerol, initiated the inflow of Ca super(2+), Mn super(2+) and Sr super(2+). Acetylcholine and thapsigargin initiated the inflow of Ca super(2+) and Mn super(2+), but not of Sr super(2+). The activation of bivalent cation inflow by OAG: (i) was mimicked by another membrane-permeant diacylglycerol analogue, 1,2-dioctanoyl-sn-glycerol, but not by the membrane-impermeant analogue 1-stearoyl-2-arachidonyl-sn-glycerol; (ii) was not blocked by staurosporin or chelerythrine, inhibitors of protein kinase C; (iii) was enhanced by RHC80267 and R50922, inhibitors of diacylglycerol lipase and diacylglycerol kinase respectively; and (iv) was inhibited by extracellular Ca super(2+). When OAG was added after acetylcholine, the effect of OAG on Ca super(2+) inflow was over-and-above that induced by acetylcholine. 2-Aminoethyl diphenylborate (2-APB) inhibited Ca super(2+) inflow initiated by either acetylcholine or thapsigargin, but not that initiated by OAG. Flufenamic acid inhibited OAG-initiated, but not acetylcholine-initiated, Ca super(2+) and Mn super(2+) inflow. OAG-initiated Ca super(2+) inflow was less sensitive to inhibition by SK&F96365 than acetylcholine-initiated Ca super(2+) inflow. In polyadenylated RNA prepared from PC12 cells, mRNA encoding TRP (transient receptor potential) proteins 1-6 was detected by reverse transcriptase (RT)-PCR, and in lysates of PC12 cells the endogenous TRP-6 protein was detected by Western blot analysis. It is concluded that PC12 cells express a diacylglycerol-activated, non-selective cation channel. Expression of this channel function correlates with expression of the TRP-3 and TRP-6 proteins, which have been shown previously to be activated by diacylglycerol when expressed heterologously in animal cells [Hofmann, Obukhov, Schaefer, Harteneck, Gudermann, and Schultz (1999) Nature (London) 397, 259-263].

L7 ANSWER 8 OF 25 LIFESCI COPYRIGHT 2009 CSA on STN
ACCESSION NUMBER: 2002:68701 LIFESCI <<LOGINID::20090530>>
TITLE: Inhibition of Reverse Transcription In Vivo by Elevated Manganese Ion Concentration
AUTHOR: Bolton, E.C.; Mildvan, A.S.; Boeke, J.D.
CORPORATE SOURCE: Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, MD 21205 USA; E-mail: jboeke@jhmi.edu
SOURCE: Molecular Cell [Mol. Cell], (20020400) vol. 9, no. 4, pp. 879-889.
ISSN: 1097-2765.
DOCUMENT TYPE: Journal
FILE SEGMENT: N; K
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Mutations in PMR1, a yeast gene encoding a calcium/manganese exporter, dramatically decrease Ty1 retrotransposition. Ty1 cDNA is reduced in pmr1 mutant cells, despite normal levels of Ty1 RNA and proteins. The transposition defect results from Mn super(2+) accumulation that inhibits reverse transcription. Cytoplasmic accumulation of Mn super(2+) in pmr1 cells may directly affect reverse transcriptase (RT) activity. Trace amounts of Mn super(2+) potently inhibit Ty1 RT and HIV-1 RT in vitro when the preferred cation, Mg super(2+), is present. Both Mn super(2+) and Mg super(2+) alone activate Ty1 RT cooperatively with Hill coefficients of 2, providing kinetic evidence for a dual divalent cation requirement at the RT active site. We propose that occupancy of the B site is the major determinant of catalytic activity and that Mn super(2+) at this site greatly reduces catalytic activity.

L7 ANSWER 9 OF 25 LIFESCI COPYRIGHT 2009 CSA on STN

ACCESSION NUMBER: 95:69976 LIFESCI <<LOGINID::20090530>>

TITLE: alpha sub(3) beta sub(1) and alpha sub(6) beta sub(1) integrins mediate laminin/merosin binding and function as costimulatory molecules for human thymocyte proliferation

AUTHOR: Chang, A.C.; Salomon, D.R.; Wadsworth, S.; Hong, M.-J.P.; Mojcik, C.F.; Otto, S.; Shevach, E.M.; Coligan, J.E.*

CORPORATE SOURCE: Lab. Mol. Struct., Build. 4, Rm. 413, NIAID/NIH, Bethesda, MD 20892-0482, USA

SOURCE: J. IMMUNOL., (1995) vol. 154, no. 2, pp. 500-510. ISSN: 0022-1767.

DOCUMENT TYPE: Journal

FILE SEGMENT: F

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Integrins comprise a superfamily of alpha beta heterodimers that serve as cell signaling as well as adhesion molecules. We demonstrate that the alpha sub(3) beta sub(1) and alpha sub(6) beta sub(1) integrins are laminin/merosin receptors expressed in human thymocytes. By reverse transcriptase-PCR analysis, we determined that the alpha sub(3A) beta sub(1), but not the alpha sub(3B) beta sub(1), cytoplasmic structural variant of alpha sub(3) beta sub(1) is expressed in thymocytes. In contrast, both alpha sub(6A) beta sub(1) and alpha sub(6B) beta sub(1) cytoplasmic structural variants of alpha sub(6) beta sub(1) are expressed. A small percentage (10 to 15%) of human thymocytes bind to immobilized laminin, and even fewer (3 to 5%) bind to merosin, the laminin isoform normally present in the thymus. This binding, however, can be increased to 39 to 41% after activation of thymocytes with Mn super(2+) (or PMA). Binding to either laminin or merosin is completely inhibited by anti- beta sub(1) mAb or by a mixture of anti- alpha sub(3) and anti- alpha sub(6) mAbs, indicating that both alpha sub(3) beta sub(1) and alpha sub(6) beta sub(1) participate in thymocyte adhesion to the laminin family of extracellular matrix proteins. The protein kinase C inhibitors, calphostin C and staurosporine, inhibit Mn super(2+)-enhanced thymocyte binding, suggesting that protein kinase C activity is crucial for the binding. Furthermore, the data indicate that at least two divalent cation binding sites serve to regulate integrin binding activity. Finally, we show that both immobilized laminin and merosin have costimulatory function for anti-CD3-induced thymocyte proliferation, and both anti- alpha sub(3) and anti- alpha sub(6) mAbs can block this proliferative response. The cooperative function of alpha sub(3) beta sub(1) and alpha sub(6) beta sub(1) evidenced in the laminin/merosin binding and proliferation assays suggests that

thymocyte-merosin interactions may play an important role in thymic T cell development.

L7 ANSWER 10 OF 25 LIFESCI COPYRIGHT 2009 CSA on STN
ACCESSION NUMBER: 93:96173 LIFESCI <<LOGINID::20090530>>
TITLE: Human cortical neuronal cell line: A model for HIV-1 infection in an immature neuronal system.
AUTHOR: Truckenmiller, M.E.; Kulaga, H.; Coggiano, M.; Wyatt, R.; Snyder, S.H.; Sweetnam, P.M.
CORPORATE SOURCE: Pfizer Cent. Res., P.O. Box 175, Eastern Point Rd., Groton, CT 06340, USA
SOURCE: AIDS RES. HUM. RETROVIRUSES., (1993) vol. 9, no. 5, pp. 445-453.
ISSN: 0889-2229.
DOCUMENT TYPE: Journal
FILE SEGMENT: V
LANGUAGE: English
SUMMARY LANGUAGE: English
AB HCN-1A is a human cerebral cortical neuronal cell line having properties consistent with cells of immature neuronal origin. This article details evidence for productive low-level infection of HCN-1A cells with human immunodeficiency virus type 1 (HIV-1). In vitro exposure to HCN-1A monolayers to a high titer of either LAV/HTLV-III sub(B) or HTLV-III sub(MN) resulted in HIV-1 p24 antigen production and a moderate increase in reverse transcriptase activity in cell-free supernatants. The cells in both LAV/HTLV-III sub(B)- and HTLV-III sub(MN)-infected cultures were passaged and proliferated as long as 5 weeks while continuing to express low levels of viral antigen. Virus-positive cells were detected by indirect immunofluorescence, using serum from an individual with acquired immune deficiency syndrome (AIDS) as well as with a gp120 monoclonal antibody. Confirmation of HCN-1A infection was provided by polymerase chain reaction analyses of both nuclear and cytoplasmic DNA and by de novo synthesis of viral proteins as shown by metabolic labeling and immunoprecipitation. Virus in cell-free supernatants from infected HCN-1A cultures was passaged to a permissive human T cell line (A3.01). HCN-1A cells had no detectable surface CD4 protein or CD4 message. However, the cells expressed the membrane glycolipids, galactocerebroside and sulfatide, possible receptors for gp120 on cells of neuronal origin. Undifferentiated HCN-1A cells provide an in vitro model for investigating potential interactions of HIV-1 with a homogeneous population of immature cortical neurons.

L7 ANSWER 11 OF 25 LIFESCI COPYRIGHT 2009 CSA on STN
ACCESSION NUMBER: 93:55264 LIFESCI <<LOGINID::20090530>>
TITLE: Potent and highly selective human immunodeficiency virus type 1 (HIV-1) inhibition by a series of alpha -anilinophenylacetamide derivatives targeted at HIV-1 reverse transcriptase.
AUTHOR: Pauwels, R.; Andries, K.; Debyser, Z.; Van Daele, P.; Schols, D.; Stoffels, P.; De Vreese, K.; Woestenborghs, R.; Janssen, P.A.J.; et al.
CORPORATE SOURCE: Rega Inst. Med. Res., Katholieke Univ. Leuven, B-3000 Leuven, Belgium
SOURCE: PROC. NATL. ACAD. SCI. USA., (1993) vol. 90, no. 5, pp. 1711-1715.
ISSN: 0027-8424.
DOCUMENT TYPE: Journal
FILE SEGMENT: N; V
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In vitro evaluation of a large chemical library of pharmacologically acceptable prototype compounds in a high-capacity, cellular -based screening system has led to the discovery of another family of human immunodeficiency virus type 1 (HIV-1) inhibitors. Through optimization of a lead compound, several alpha -anilinophenylacetamide (alpha -APA) derivatives have been identified that inhibit the replication of several HIV-1 strains (III sub(B)/LAI, RF, NDK, MN , HE) in a variety of host cell types at concentrations that are 10,000- to 100,000-fold lower than their cytotoxic concentrations. THe IC sub(50) of the alpha -APA derivative R 89439 for HIV-1 cytopathicity in MT-4 cells was 13 nM. The median 90% inhibitory concentration (IC sub(90)) in a variety of host cells was 50-100 nM. Although these alpha -APA derivatives are active against a tetrahydroimidazo (4,5,1-jk)(1,4)benzodiazepin-2(1H)-thione-(TIBO)-resistant HIV-1 strain, they do not inhibit replication of HIV-2 (strains ROD and EHO) or simian immunodeficiency virus (strains Mac251, mndGB1, and agm3). An HIV-1 strain containing the Tyr super(181) arrow right Cys mutation in the reverse transcriptase region displayed reduced sensitivity. alpha -APA derivative R 89439 inhibited virion and recombinant reverse transcriptase of HIV-1 but did not inhibit that of HIV-2.

L7 ANSWER 12 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:37363058 BIOTECHNO <<LOGINID::20090530>>
TITLE: Cholesterol Depletion Impairs Vascular Reactivity to Endothelin-1 by Reducing Store-Operated Ca.sup.2.sup.+ Entry Dependent on TRPC1
AUTHOR: Bergdahl A.; Gomez M.F.; Dreja K.; Xu S.-Z.; Adner M.; Beech D.J.; Broman J.; Hellstrand P.; Sward K.
CORPORATE SOURCE: Dr. K. Sward, Department of Physiological Sciences, Lund University, BMC F12, S-21 84 Lund, Sweden. E-mail: karl.sward@mphy.lu.se
SOURCE: Circulation Research, (31 OCT 2003), 93/9 (839-847), 30 reference(s)
CODEN: CIRUAL ISSN: 0009-7330
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37363058 BIOTECHNO <<LOGINID::20090530>>
AB The reactivity of the vascular wall to endothelin-1 (ET-1) is influenced by cholesterol, which is of possible importance for the progression of atherosclerosis. To elucidate signaling steps affected, the cholesterol acceptor methyl-β-cyclodextrin (mβcd, 10 mmol/L) was used to manipulate membrane cholesterol and disrupt caveolae in intact rat arteries. In endothelium-denuded caudal artery, contractile responsiveness to 10 nmol/L ET-1 (mediated by the ET.sub.A receptor) was reduced by mβcd and increased by cholesterol. Neither ligand binding nor colocalization of ET .sub.A and caveolin-1 was affected by mβcd. Ca.sup.2.sup.+ inflow via store-operated channels after depletion of intracellular Ca.sup.2.sup.+ stores was reduced in mβcd-treated caudal arteries, as shown by Mn .sup.2.sup.+ quench rate and intracellular [Ca.sup.2.sup.+] response. Expression of TRPC1, 3, and 6 was detected by reverse transcriptase-polymerase chain reaction, and colocalization of TRPC1 with caveolin-1 was reduced by mβcd, as seen by immunofluorescence. Part of the contractile response to ET-1 was inhibited by Ni.sup.2.sup.+ (0.5 mmol/L) and by a TRPC1 blocking antibody. In the basilar artery, exhibiting less store-operated channel activity than the caudal artery, ET-1-induced contractions were insensitive to the TRPC1 blocking antibody and to mβcd.

Increased store-operated channel activity in basilar arteries after organ culture correlated with increased sensitivity of ET-1 contraction to mβcd. These results suggest that cholesterol influences vascular reactivity to ET-1 by affecting the caveolar localization of TRPC1.

L7 ANSWER 13 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36994634 BIOTECHNO <<LOGINID::20090530>>
TITLE: Cloning and characterization of a mouse endoplasmic reticulum alkaline ceramidase. An enzyme that preferentially regulates metabolism of very long chain ceramides
AUTHOR: Mao C.; Xu R.; Szulc Z.M.; Bielawski J.; Beeker K.P.; Bielawska A.; Galadari S.H.; Hu W.; Obeid L.M.
CORPORATE SOURCE: C. Mao, Div. of General Internal Medicine, 114 Doughty St., Charleston, SC 29425, United States.
E-mail: maoc@musc.edu
SOURCE: Journal of Biological Chemistry, (15 AUG 2003) , 278/33 (31184-31191), 30 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36994634 BIOTECHNO <<LOGINID::20090530>>
AB Ceramidases deacylate ceramides, important intermediates in the metabolic pathway of sphingolipids. In this study, we report the cloning and characterization of a novel mouse alkaline ceramidase (maCER1) with a highly restricted substrate specificity. maCER1 consists of 287 amino acids, and it has a 28 and 32% identity to the Saccharomyces alkaline ceramidases (YPC1p and YDC1p) and the human alkaline phytoceramidase, respectively. Reverse transcriptase-PCR analysis demonstrated that maCER1 was predominantly expressed in skin. maCER1 was localized to the endoplasmic reticulum as revealed by immunocytochemistry. In vitro biochemical characterization determined that maCER1 hydrolyzed D-erythro-ceramide exclusively but not D-erythro-dihydroceramide or D-ribo-phytoceramide. Similar to other alkaline ceramidases, maCER1 had an alkaline pH optimum of 8.0, and it was activated by Ca.sub.2.sub.+ but inhibited by Zn.sup.2.sup.+, Cu.sup.2.sup.+, and Mn .sup.2.sup.+. maCER1 was also inhibited by sphingosine, one of its products. Metabolic labeling studies showed that overexpression of maCER1 caused a decrease in the incorporation of radiolabeled dihydrosphingosine into ceramide and complex sphingolipids but led to a concomitant increase in sphingosine-1-P (S1P) in HeLa cells. Mass measurement showed that overexpression of maCER1 selectively lowered the cellular levels of D-erythro-C.sub.2.sub.4.sub.:.sub.1-ceramide, but not other ceramide species and caused an increase in the levels of S1P. Taken together, these data suggest that maCER1 is a novel alkaline ceramidase with a stringent substrate specificity and that maCER1 is selectively expressed in skin and may have a role in regulating the levels of bioactive lipids ceramide and S1P, as well as complex sphingolipids.

L7 ANSWER 14 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36262591 BIOTECHNO <<LOGINID::20090530>>
TITLE: Comparative analysis of apoptosis-inducing activity of codeine and codeinone
AUTHOR: Hitosugi N.; Hatsukari I.; Ohno R.; Hashimoto K.; Mihara S.; Mizukami S.; Nakamura S.; Sakagami H.; Nagasaka H.; Matsumoto I.; Kawase M.

CORPORATE SOURCE: Dr. N. Hitosugi, Department of Anesthesiology, Meikai Univ. School of Dentistry, Sakado, Saitama 350-0283, Japan.
E-mail: nao-hito@rc4.so-net.ne.jp
SOURCE: Anesthesiology, (01 MAR 2003), 98/3 (643-650), 41 reference(s)
CODEN: ANESAV ISSN: 0003-3022
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36262591 BIOTECHNO <<LOGINID::20090530>>
AB Background: There are relatively few studies about the antiproliferative effects of codeine-related compounds on human cancer cell lines, compared with those of morphine-related compounds. The authors previously found that codeinone, an oxidation metabolite of codeine, among 10 opioids, showed the highest cytotoxic activity (DNA fragmentation-inducing activity) against human promyelocytic leukemic cell lines (HL-60). This was counteracted by an antioxidant, N-acetyl-L-cysteine (NAC). These findings prompted us to perform a more detailed study of apoptosis induction after codeinone treatment. Methods: Apoptosis was induced by treating HL-60 cells for 1-6 h with codeine or codeinone. DNA fragmentation was assessed by both agarose gel electrophoresis and fluorometric determination of the fragmented DNA after staining with diamidinophenylindole (DAPI). The appearance of apoptotic cells was monitored by microscopic observation after staining with Hoechst (H)-33342, and fluorescence activated cell sorter (FACS) after staining with Annexin. The release of cytochrome c and cytochrome oxidase from mitochondria and activation of caspase 3 were monitored by Western blot analysis. Intracellular caspase 3-like activity was confirmed by FACS, using cell permeable substrate. Mitochondrial manganese -containing superoxide dismutase (MnSOD) activity and mRNA expression were assayed by activity staining after separation on the polyacrylamide gel electrophoresis, and reverse transcriptase-polymerase chain reaction (RT-PCR), respectively. Results: Codeinone induced internucleosomal DNA fragmentation and production of Annexin-positive apoptotic cells more potently than codeine in HL-60 cells. Codeinone stimulated the release of both cytochrome c and cytochrome oxidase, and cleavage of procaspase 3 without significant changes in both the activity and expression of MnSOD. Conclusions: Codeinone was found to possess both apoptosis and necrosis-inducing activity, in addition to the reported antinociceptive activity, further substiating its antitumor potential.

L7 ANSWER 15 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:34311540 BIOTECHNO <<LOGINID::20090530>>
TITLE: Scavenger receptor class B type I expression and elemental analysis in cerebellum and parietal cortex regions of the Alzheimer's disease brain
AUTHOR: Srivastava R.A.K.; Jain J.C.
CORPORATE SOURCE: R.A.K. Srivastava, Cellular and Molecular Biology, Esperion Therapeutics Inc., 3621 S State Street, Ann Arbor, MI 48108, United States.
E-mail: ajits@esperion.com
SOURCE: Journal of the Neurological Sciences, (15 APR 2002), 196/1-2 (45-52), 51 reference(s)
CODEN: JNSCAG ISSN: 0022-510X
PUBLISHER ITEM IDENT.: S0022510X02000266
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: Netherlands
LANGUAGE: English

SUMMARY LANGUAGE: English
AN 2002:34311540 BIOTECHNO <<LOGINID::20090530>>
AB Metal ions play an important role in health and disease by influencing cellular biochemical pathways. The increased concentrations of some metal ions may have cytotoxic effects through their ability to oxidatively modify biomolecules, which may cause oxidative stress-induced brain cell death leading to neurodegenerative disorders observed in Alzheimer's disease (AD). We therefore performed elemental analysis of human brain tissues by a sophisticated method of inductively coupled plasma mass spectrometry (ICP-MS) in two regions of the AD brain, the parietal cortex and cerebellum, and compared them with the age-matched control. Our analysis shows the differential distribution of some metal ions in the two regions of the brain. Most importantly, Si, Sn, Al and Mn showed significantly higher levels in the parietal cortex of the AD brain compared to the control. The other metal ions showing moderate increases in the parietal cortex were Na, Te, Cr, Fe and B. Since these metal ions can modify lipoproteins in the brain and modified lipoproteins are taken up by scavenger receptors class B type I (SR-BI), we also determined the presence of SR-BI in the parietal cortex and cerebellum regions of the control and AD brains using a sensitive method, the reverse transcriptase-polymerase chain reaction. Our results suggest that SR-BI are present in the parietal cortex as well as in the cerebellum of the control and AD brains, suggesting that the presence of SR-BI may be involved in the uptake of oxidatively modified lipoproteins and β-amyloid (Aβ) protein complexed with apoE, suggesting implications in the progression of late onset AD and other neurodegenerative disorders characterized by the deposition of insoluble aggregates observed in the AD brain.

=> d L7 ibib abs 16-25

L7 ANSWER 16 OF 25 BIOTECHNO
ACCESSION NUMBER: 2002:34212610 BIOTECHNO <<LOGINID::20090530>>
TITLE: Homocysteine induces 3-hydroxy-3-methylglutaryl coenzyme a reductase in vascular endothelial cells: A mechanism for development of atherosclerosis?
AUTHOR: Li H.; Lewis A.; Brodsky S.; Rieger R.; Iden C.; Goligorsky M.S.
CORPORATE SOURCE: Dr. H. Li, Department of Medicine, State University of New York, Stony Brook, NY 11794-8152, United States. E-mail: hongli888@yahoo.com
SOURCE: Circulation, (05 MAR 2002), 105/9 (1037-1043), 35 reference(s)
CODEN: CIRCAZ ISSN: 0009-7322
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34212610 BIOTECHNO <<LOGINID::20090530>>
AB Background - It has been established that hyperhomocyst(e)inemia (HHCy) is an independent and graded risk factor for atherosclerosis, although the molecular link to the atherosclerotic process remains obscure. Methods and Results - Screening human umbilical vein endothelial cells (HUVECs) with complementary DNA microarray for the gene expression modified by homocysteine (Hcy) revealed that 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) was upregulated. This effect was confirmed using quantitative reverse transcriptase-polymerase chain reaction. Actinomycin D studies revealed that

Hcy stabilized HMGCR mRNA (τ.sub.1.sub./.sub.2, 9.5±1.0 versus 5.0±0.2 hours). Expression of immunodetectable HMGCR in both HUVECs and renal microvascular endothelial cells was increased in Hcy-treated cells in association with the increased abundance of caveolin. Application of a cell-permeable superoxide dismutase mimetic, Mn-TBAP, reversed the Hcy-induced expression of HMGCR. Additional biochemical analysis of the abundance of total cellular cholesterol showed that 0, 20, 50, and 100 μmol/L Hcy resulted in 22.2±7.3%, 39.5±1.2%, and 50.4±6.8% increase , respectively. Gas chromatography mass spectrometry analysis of extracted cholesterol from Hcy-treated HUVECs and from the culture medium showed 17.8±5.2% and 24.0±14.5% increases, respectively. Application of simvastatin to Hcy-treated cells reduced cellular cholesterol and prevented Hcy-induced suppression of NO production by HUVECs in a dose-dependent manner. Conclusions - Using a cDNA microarray, the data disclosed an unexpected link between Hcy and cholesterol dysregulation based on the finding of increased abundance of HMGCR mRNA and protein in endothelial cells, demonstrated the possible role of Hcy-induced oxidative stress in this response, and revealed the improvement of endothelial NO production in Hcy-treated HUVECs by statins. Collectively, these findings may provide a solid explanation for the observed proatherogenic effect of HHcy.

L7 ANSWER 17 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32763153 BIOTECHNO <<LOGINID::20090530>>
TITLE: Maitotoxin activates an endogenous non-selective cation channel and is an effective initiator of the activation of the heterologously expressed hTRPC-1 (transient receptor potential) non-selective cation channel in H4-IIE liver cells
AUTHOR: Brereton H.M.; Chen J.; Rychkov G.; Harland M.L.; Barritt G.J.
CORPORATE SOURCE: G.J. Barritt, Department of Medical Biochemistry, School of Medicine, Flinders University, G.P.O. Box 2100, Adelaide, SA 5001, Australia.
E-mail: greg.barritt@flinders.edu.au
SOURCE: Biochimica et Biophysica Acta - Molecular Cell Research, (22 AUG 2001), 1540/2 (107-126), 53 reference(s)
CODEN: BAMRDP ISSN: 0167-4889
PUBLISHER ITEM IDENT.: S0167488901001240
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32763153 BIOTECHNO <<LOGINID::20090530>>
AB The structures and mechanisms of activation of non-selective cation channels (NSCCs) are not well understood although NSCCs play important roles in the regulation of metabolism, ion transport, cell volume and cell shape. It has been proposed that TRP (transient receptor potential) proteins are the molecular correlates of some NSCCs. Using fura-2 and patch-clamp recording, it was shown that the maitotoxin-activated cation channels in the H4-IIE rat liver cell line admit Ca.sup.2.sup.+, Mn.sup.2.sup.+ and Na.sup.+, have a high selectivity for Na.sup.+ compared with Ca.sup.2.sup.+, and are inhibited by Gd.sup.3.sup.+ (half-maximal inhibition at 1 μM). Activation of the channels by maitotoxin was inhibited by increasing the extracellular Ca.sup.2.sup.+ concentration or by inclusion of 10 mM EGTA in the patch pipette. mRNA encoding TRP proteins 1, 2 and 3 at levels comparable with those in brain was detected using reverse transcriptase-polymerase chain

reaction in poly(A).sup.+ RNA prepared from H4-IIE cells and freshly-isolated rat hepatocytes. In H4-IIE cells transiently transfected with cDNA encoding hTRPC-1, the expressed hTRPC-1 protein was chiefly located at intracellular sites and at the plasma membrane. Cells expressing hTRPC-1 exhibited a substantial enhancement of maitotoxin-initiated Ca.sup.2.sup.+ inflow and a modest enhancement of thapsigargin-initiated Ca.sup.2.sup.+ inflow (measured using fura-2) and no enhancement of the highly Ca.sup.2.sup.+-selective store-operated Ca.sup.2.sup.+ current (measured using patch-clamp recording). In cells expressing hTRPC-1, maitotoxin activated channels which were not found in untransfected cells, have an approximately equal selectivity for Na.sup.+ and Ca.sup.2.sup.+, and are inhibited by Gd.sup.3.sup.+ (half-maximal inhibition at 3 μM). It is concluded that in liver cells (i) maitotoxin initiates the activation of endogenous NSCCs with a high selectivity for Na.sup.+ compared with Ca.sup.2.sup.+; (ii) TRP proteins 1, 2 and 3 are expressed; (iii) maitotoxin is an effective initiator of activation of heterologously expressed hTRPC-1 channels; and (iv) the endogenous TRP-1 protein is unlikely to be the molecular counterpart of the maitotoxin-activated NSCCs nor the highly Ca.sup.2.sup.+-selective store-operated Ca.sup.2.sup.+ channels.

L7 ANSWER 18 OF 25 BIOTECHNO COPYRIGHT 2009 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25138286 BIOTECHNO <<LOGINID::20090530>>
TITLE: Integrin α2 I-domain is a binding site for collagens
AUTHOR: Tuckwell D.; Calderwood D.A.; Green L.J.; Humphries M.J.
CORPORATE SOURCE: School of Biological Sciences, University of Manchester, Stopford Building, Oxford Road,Manchester M13 9PT, United Kingdom.
SOURCE: Journal of Cell Science, (1995), 108/4 (1629-1637)
CODEN: JNCSAI ISSN: 0021-9533
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25138286 BIOTECHNO <<LOGINID::20090530>>
AB Integrins α1β1 and α2β1 are major cellular receptors for collagens. The α1 and α2 subunits contain a .sim. 200 amino acid inserted domain (I-domain) in their N-terminal region and, because of the homology between the I-domains and the collagen-binding A-domains of von Willebrand factor, it has been suggested that the I-domains might mediate the collagen-binding functions of α1β1 and α2β1. In order to fully investigate this hypothesis, we have generated recombinant human α2 I-domain (rα2I) by reverse transcriptase-polymerase chain reaction/bacterial expression and tested its ability to mediate the collagen-binding functions of α2β1. Rα2I binds specifically to type I collagen in a concentration-dependent manner: binding is cation dependent and, like the complete receptor, is supported by magnesium and manganese ions but not by calcium ions. Rα2I is recognised by anti-functional anti-α2 monoclonal antibodies 6F1, 5E8 and P1E6 in capture ELISAs, and anti-functional antibodies inhibited rα2I-collagen binding. In addition, rα2I inhibits cell spreading on collagen. Rα2I is therefore a collagen-binding domain and can account for many of the collagen-binding functions of integrin α2β1. We have also determined the collagen specificity of rα2I and found that it binds types I, II and XI collagen.

L7 ANSWER 19 OF 25 ADISNEWS COPYRIGHT (C) 2009 Adis Data Information BV on STN
ACCESSION NUMBER: 1995:282 ADISNEWS <<LOGINID::20090530>>
ENTRY DATE: Entered STN: 8 Aug 2001
Last Updated on STN: 8 Aug 2001
DOCUMENT NUMBER: 11738324-800314554
TITLE: Product news: Proposed HIV defenses: inner and outer.
SOURCE: INPHARMA 25 Jul 1995 ISSN: 1173-8324
DOCUMENT TYPE: (MIX)
WORD COUNT: 370

L7 ANSWER 20 OF 25 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1995-02667 BIOTECHDS <<LOGINID::20090530>>
TITLE: Inhibition of human immunodeficiency virus-type 1 (HIV-1) infection in vitro after intracellular expression of an antibody fragment directed against reverse transcriptase; HIV virus-1 reverse-transcriptase monoclonal antibody variable heavy and light chain gene expression in MOLT-3 SupT-1 cell culture for intracellular immunization (conference abstract)
AUTHOR: Weichold F F; Maciejewski J P; Gallo R C; Reitz M; Young N S
CORPORATE SOURCE: Nat.Heart-Lung+Blood-Inst.Bethesda; Nat.Cancer-Inst.Bethesda
LOCATION: Hematology Branch, National Heart, Blood and Lung Institute, Bethesda, MD 20892, USA.
SOURCE: Blood; (1994) 84, 10, 248a
CODEN: BLOOAW
ISSN: 0006-4971
American Society of Hematology, 36th Annual Meeting, Nashville, TN, 2-6 December, 1994.
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1995-02667 BIOTECHDS <<LOGINID::20090530>>
AB A novel strategy of intracellular immunization (II) was tested to block HIV virus-1 infection. Oligonucleotide primers were synthesized for genes encoding the VH and VL chains of a monoclonal antibody to the reverse-transcriptase (RT, EC-2.7.7.49) of HIV virus-1. Cloned genes were inserted into an Epstein-Barr virus-based episomal expression vector containing a selectable marker. Vectors were introduced into HIV-1-permissive MOLT-3 and SupT-1 cells by electroporation. Antibody fragments were detected with rabbit antibodies directed to mouse IgG H and L chains. After infection with HIV-1 IIIB and RF and low passage clinical isolates MN and 571, p24 gag production was detected by ELISA at 3 days, but little or no p24 was found after this for a period of 30 day post-infection, or after reinoculation with fresh HIV-1. A 103-fold decrease in both viral DNA and double LTR circular DNA was estimated in cell cultures containing the VH and VL plasmids compared to control. Intracellular expression of active anti-RT F(ab) inhibits HIV-1 propagation in vitro. Gene transfer mediated II might be a feasible treatment strategy. (0 ref)

L7 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:117443 CAPLUS <<LOGINID::20090530>>
DOCUMENT NUMBER: 114:117443
ORIGINAL REFERENCE NO.: 114:19889a,19892a
TITLE: Some yeast proteins are recognized by antibodies to reverse transcriptases from several mammalian retroviruses and display reverse transcriptase activity
AUTHOR(S): Hallbreich, A.

CORPORATE SOURCE: Lab. Physiol. Cell., Univ. Pierre et Marie Curie, Paris, 75005, Fr.
SOURCE: Biochemistry International (1990), 22(5), 859-66
CODEN: BIINDF; ISSN: 0158-5231
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antibodies directed against reverse transcriptases (RT) of the mammalian retroviruses SSV and RD114 specifically recognize on Western blots yeast cytoplasmic soluble proteins of 31 and 45 kDa and inhibit RT activity in this fraction. Anti-RLV (Rous leukemia virus) RT IgG recognizes a protein of 40-43 kDa in the particulate (VLP) fraction and inhibits RT activity in it. No inhibition of RT activity was seen with normal serum, anti-AMV (avian myeloblastosis virus) RT IgG or antisera against yeast DNA polymerase I and DNA polymerase III. These yeast RTs display RNase H activity and are not inhibited by aphidicolin. They prefer Mn2+ as cofactor over Mg2+ display an optimum temperature of 25-30° and are expressed in a diploid as well as 2 haploid strains and are thus distinct from yeast Ty encoded RTs.

L7 ANSWER 22 OF 25 CIN COPYRIGHT 2009 ACS on STN
AB A new study suggests an entirely new way to inhibit HIV's reverse transcriptase enzyme: by dousing it with manganese ions. Researchers at Johns Hopkins University have found that high levels of manganese prevent reverse transcriptase from performing its function. since intracellular manganese levels are under the control of certain transporter molecules, those could be targets from novel drugs aimed at disabling reverse transcriptase.

L7 ANSWER 23 OF 25 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 2003:33140 DISSABS Order Number: AAI3068121
TITLE: Replication of the Ty1 retrotransposon in Saccharomyces cerevisiae
AUTHOR: Bolton, Eric Christopher [Ph.D.]; Boeke, Jef D. [adviser]
CORPORATE SOURCE: The Johns Hopkins University (0098)
SOURCE: Dissertation Abstracts International, (2003) Vol. 63, No. 10B, p. 4494. Order No.: AAI3068121. 163 pages. ISBN: 0-493-87646-4.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
AB The identification of the critical components of the Ty1 RNA and element-encoded proteins has allowed and will continue to allow detailed in vivo genetic studies and biochemical characterization in vitro. Genetic and biochemical studies of the replication of the Ty1 retrotransposon in Saccharomyces cerevisiae are described here. We describe a modular mini-Ty1 element encoding the minimal sequence capable of being retrotransposod by the Ty1 proteins, supplied in trans by a helper construct. Using a genetic screening strategy, we recovered transposition-deficient modular mini-Ty1-HIS3 elements; many of these possessed mutations in sequences required in cis for Ty1 replication and integration. Moreover, two distinct clusters of mutations mapped to the GAGGAGA sequence at the extreme 5' end of the Ty1 transcript and the complementary downstream UCUCCUC sequence, 264 nucleotides into the RNA. Disruption of the reverse complementarity of these two sequences decreased Ty1 cDNA accumulation and transposition, despite normal levels of Ty1 RNA and proteins. Restoration of complementarity rescued cDNA production and transposition to wild-type levels. We propose that the interaction between the 5' GAGGAGA and UCUCCUC sequences allows Ty1 RNA to form a dimeric structure, similar to but structurally distinct from the

retroviral "kissing-loop" dimerization motif.

We show that mutations in PMR1, a yeast gene encoding a calcium/manganese exporter, dramatically decrease Ty1 retrotransposition. Ty1 cDNA is reduced in pmr1 mutant cells, despite normal levels of Ty RNA and proteins. The transposition defect results from Mn2+ accumulation, which in turn inhibits reverse transcription. Intracellular accumulation of Mn2+ in pmr1 cells directly affects Ty 1 reverse transcriptase (RT) activity. Trace amounts of Mn2+ potently inhibit Ty1 RT and HIV-1 RT in vitro when the preferred cation, Mg2+, is present in saturating amounts. Both Mn2+ and Mg2+ alone activate Ty1 RT cooperatively with Hill coefficients of 2, providing strong kinetic evidence for a dual divalent cation requirement at the RT active site. These findings emphasize the importance of metal ion clusters in catalysis and suggest a novel class of RT inhibitors, based on alteration of intracellular metal ion concentrations.

L7 ANSWER 24 OF 25 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 1998:47096 PROMT <<LOGINID::20090530>>
TITLE: HIV Gene Therapy "Nucleic Acid-Based Therapies Against HIV."
SOURCE: Vaccine Weekly, (26 Jan 1998) pp. N/A.
ISSN: 1074-2921.
LANGUAGE: English
WORD COUNT: 307
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB K. Moelling, B. Strack, J. Jendis and J. Heinrich. Institute of Medical Virology of the University of Zurich, Zurich, Switzerland. According to an abstract submitted by the authors to the Sixth European Conference on Clinical Aspects and Treatment of HIV Infection, held October 11-15, 1997, in Hamburg, Germany, "DNA vaccines hold great promise for prevention and immunotherapy of viral, parasitic infections and cancer. Preclinical studies have recently shown that polynucleotides coding for proteins from pathogens are effective means to generate cellular and humoral responses without the potential risk of live virus. An HIV-1 DNA vaccine coding for the HIV-1 modified env gene from an MN isolate and rev Has been applied to HIV-1 infected individuals in Philadelphia and in February 1996 in Zurich. A clinical trial with uninfected healthy volunteers has been initiated. A DNA vaccine against HIV nucleoprotein and gag as well as malignant melanoma is under investigation in preclinical animal studies, including models for metastases. The efficiency of nucleic acid vaccination can be improved by coexpression of costimulators of immunomodulators. Some plasmid designs have been made using IRKS for compression for B7, GM-CSF or IL-12, and will be discussed. The molecular mechanism of activation is not well understood. Mice with various genetic backgrounds including knock-out mice lacking e.g. CD8 cells are under investigation. Furthermore, a highly conserved polypurine tract, PPT, on the viral RNA which serves as primer for plus-strand DNA synthesis by the retroviral reverse transcriptase (RT), is a possible target for triple-helix formation. This has been analyzed with a triplex-forming oligodeoxynucleotide which has been shown to inhibit the RT and the RNaseH in vitro and against replication of clinical HIV isolates in culture. Preliminary data obtained by PCR indicate that DNA provirus formation inside the cells is inhibited. Furthermore, stable expression of an oligonucleotide from a transduced retroviral vector is under investigation."

L7 ANSWER 25 OF 25 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on

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ACCESSION NUMBER: 1997:536870 SCISEARCH <<LOGINID::20090530>>
THE GENUINE ARTICLE: XK718
TITLE: Inhibition of replication of HIV in primary monocyte/macrophages by different antiviral drugs and comparative efficacy in lymphocytes
AUTHOR: Aquaro S (Reprint); Perno C F; Balestra E; Balzarini J; Cenci A; Francesconi M; Panti S; Serra F; Villani N; Calio R
CORPORATE SOURCE: UNIV ROMA TOR VERGATA, DEPT EXPT MED & BIOCHEM SCI, I-00135 ROME, ITALY; CATHOLIC UNIV LEUVEN, REGA INST MED RES, B-3000 LOUVAIN, BELGIUM; FRASCATI HOSP, HAEMATOL CTR, FRASCATI, ITALY
COUNTRY OF AUTHOR: ITALY; BELGIUM
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (JUL 1997) Vol. 62, No. 1, pp. 138-143.
ISSN: 0741-5400.
PUBLISHER: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Several anti-HIV drugs acting on different steps of virus replication were tested in our experimental model of primary monocyte/macrophages; the results were compared with the activity found in lymphocytes, Nucleoside analogues (AZT, ddI, ddC, d4T, PMEA, 3TC etc.) show greater,activity in macrophages (M/M) than in lymphocytes. In particular, the EC50 of AZT, ddC, and ddI in M/M is 2- to 100-fold lower than that found in lymphocytes, This greater efficacy of nucleoside analogues in M/M depends on the enhancement of their chain-terminating activity by the low levels of endogenous deoxynucleoside-triphosphates (dNTP) usually found in resting cells such as MN, Nonnucleoside reverse transcriptase inhibitors (NNRTI) do not act as chain terminators (thus their antiviral effect is not related to the intracellular concentrations of dNTP); as a consequence the activity of TSAO, HEPT, TIBO, and other NNRTI tested in M/M is similar to that found in lymphocytes. Regarding inhibitors of binding and fusion of HN; we found that their anti-HIV activity is markedly decreased (or even nullified) when M/M are treated with cytokine activators of M/M function and enhancers of HIV replication, More relevant from a clinical standpoint, protease inhibitors are able to inhibit HIV replication in chronically infected macrophages (i.e., cells carrying the proviral genome already integrated in the host genome), All other inhibitors of late stage of virus life cycle tested (antisense-rev, anti-tat, interferon-alpha and -gamma, phosphorothioate analogues, GLQ-223, etc.) were totally inactive in chronically infected macrophages, The different effects of various classes of HIV inhibitors in lymphocytes and macrophages suggests that AIDS therapy should consider all aspects of the pathogenesis of HIV infection and must be restricted to drugs, or combinations of drugs, active against both lymphocytes and M/M in all body compartments where the virus hides and replicates.

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